

WE CLAIM:

1. A method for inhibiting restenosis associated with mechanical treatment of a blood vessel in a mammal comprising:

introducing a polynucleotide to said blood vessel after said mechanical treatment, said polynucleotide comprising a thymidine kinase gene;

expressing said thymidine kinase gene to produce thymidine kinase protein in cells of said blood vessel; and

then administering to said mammal an effective amount of a DNA replication-inhibiting nucleoside analog capable of being phosphorylated by said thymidine kinase protein and preferentially incorporating said phosphorylated analog into the DNA of proliferating cells, whereby said proliferating cells are killed.

2. The method of Claim 1, wherein said mechanical treatment is balloon angioplasty, laser, atherectomy device or stent implantation.

3. The method of Claim 1, wherein said thymidine kinase gene is in a eukaryotic expression vector.

4. The method of Claim 3 wherein said expression vector is in a viral vector.

5. The method of Claim 4 wherein said viral vector is an adenoviral vector.

6. The method of Claim 5 further comprising a polyoma virus enhancer upstream of said thymidine kinase gene.

7. The method of Claim 6, further comprising adenoviral vector enhancer elements, encapsidation signals, origins of replication and other necessary adenoviral genes.

8. The method of Claim 7 wherein said adenoviral vector is Ad.HSV-tk.

9. The method of Claim 8 wherein said expression vector containing said thymidine kinase gene is complexed with a nonviral vector.

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10. The method of Claim 9, wherein said nonviral vector is a liposome.

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11. The method of Claim 9, wherein said nonviral vector is a receptor ligand and said expression vector-ligand complex binds to the receptor.

12. The method of Claim 1, wherein said suicide compound is ganciclovir or acyclovir.

13. The method of Claim 1, wherein said modification is phosphorylation.

14. The method of Claim 13, wherein said phosphorylated compound is further phosphorylated by cellular enzymes.

15. The method of Claim 14, wherein said phosphorylated compound is preferentially incorporated into the DNA of rapidly dividing cells.

16. A method for inhibiting restenosis associated with mechanical treatment of a blood vessel in a mammal comprising:

introducing a polynucleotide to said blood vessel after said mechanical treatment, said polynucleotide comprising a cytosine deaminase gene;

expressing said cytosine deaminase gene to produce cytosine deaminase protein in cells of said blood vessel; and

then administering to said mammal an effective amount of a DNA replication-inhibiting nucleoside analog capable of being phosphorylated by said cytosine deaminase protein and preferentially incorporating said phosphorylated analog into the DNA of proliferating cells, whereby said proliferating cells are killed.

17. The method of Claim 16, wherein said nucleoside analog is 5-fluorocytosine.

18. A recombinant adenoviral vector Ad.HSV-tk comprising:

a wild type adenovirus wherein the E3 region and about 9 map units have been deleted; and

a HSV-tk expression cassette inserted into said deleted region, wherein said expression cassette comprises the herpes simplex virus thymidine kinase gene operably linked to promoter, enhancer, encapsidation signal and origin of replication elements.

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19. The vector of Claim 18, wherein said wild type adenovirus is type 5.

20. The vector of Claim 19, wherein said elements are derived from polyoma virus and adenovirus.

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